

Design of Safe Energetic Processes Using the Advanced Flow Reactor

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1.0 Introduction

Conventional manufacturing of energetic materials includes the use of batch and semi-batch reactors. These methods offer flexibility at the cost of safety, reproducibility and often times higher cost products. Continuous processing is superior with respect to safety, reproducibility and always offers the lowest cost product. In addition, continuous processing affords 'enabling chemistry' that is often not realized in batch processing; energetic products can show instabilities in reaction mixtures making scale-up in batch reactors undesirable and extremely hazardous. Corning Incorporated has a long history of producing and commercializing products (e.g. light bulbs, Pyrex® glass, silicones, television tubes, ceramics, LCD glass) including a recent product called the Advanced-Flow™ Reactor (AFR). The reactors are particularly appealing for energetic materials production because they are made from glass and ceramic, making them corrosion resistant, designed for high performance mass and heat transfer (often challenges with energetic reactions), and engineered for seamless scale-up, which continuously plagues batch reactions, from kilo-lab to thousands of tons per year. Corning offers technology ranging from lab-scale to full manufacturing. Nalas Engineering is currently developing commercial processes to non-energetic materials using the AFR technology and proposes to utilize it as an enabling method of processing energetic materials in a timely, safe and efficient manner for evaluating novel energetic materials.

2.0 Background

Corning introduced the AFR technology in 2002 with concept development. In 2006, Corning launched the G1 reactor, which afforded small volume and capability for process development and optimization. In 2008 the G2 was launched, becoming the first AFR capable of continuous production of large amounts of chemicals. In 2009 the first G4 system was commissioned with capacity exceeding 300 kg/hr. The technology is mature and currently utilized throughout industry. The systems offer a synergy of chemistry, safety and efficient manufacturing.

3.0 Objective

The synthesis route to LLM-105 uses 2,6-diaminopyrazine-1-oxide (DAPO). The objective of this work is to demonstrate the feasibility of making LLM-105 using the AFR. In this process (Figure 1), DAPO is added to oleum or sulfuric acid, after which nitric acid is metered in slowly. The final reaction mixture is added to a warm water quench and produces LLM-105 solids. The solids isolated by filtration are washed, returned to the reactor, re-slurried in water at 70 °C, filtered, and then dried to ensure purity and potency are >99%. The reaction of DAPO to LLM-105 is exothermic and would require dose rates over hours at larger scales using semi-batch

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processing; batch reactors have poor overall heat transfer due to the low ratio of heat transfer surface area to the reactor volume. The AFR provides excellent mixing and heat transfer not feasible with the semi-batch process and affords a true commercial manufacturing option for exothermic reactions. Nalas used optimal reaction conditions identified in previous efforts in tandem with kinetic data to develop a process model for the AFR-LF configuration. Nalas recently generated proposed material specifications for LLM-105 produced from DAPO; the resulting product will be compared against this proposed specification as a measure of the success of the process.

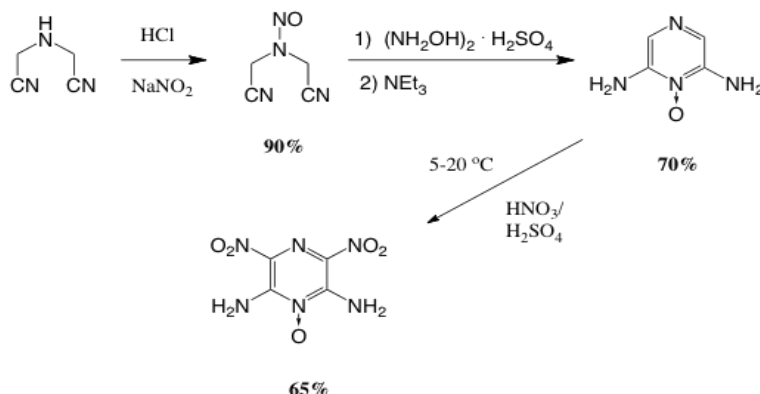


Figure 1. LLM-105 reaction scheme using DAPO

4.0 Technical Approach

Nalas utilized an eleven-plate glass module AFR system and three double diaphragm pumps (two pumps for mixed acid and a single pump for DAPO/sulfuric acid solution) for this work. The nitric acid was introduced to the reaction at two different feed locations along the length of the reactor. Previous LLM-105 synthesis work has shown the benefit of limiting the nitronium ion concentration across the reaction to maximize yield. Our model indicated that a third feed location would have been beneficial, but two feeds were utilized to reduce complexity for the initial experiments. Figure 2 below offers a visual depiction of the reactant feed configuration in the AFR.

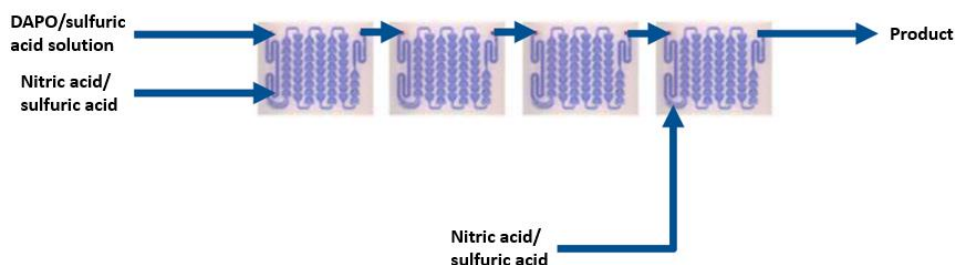


Figure 2. LLM-105 feed setup in AFR

The pump setpoints were selected to maintain the molar equivalents of all components at the desired ratio. The AFR system was tested extensively for accurate flow rates of each pump. This was accomplished by metering each acid from a container on a precision scale. All three feed pump scales were configured to communicate with the Mettler Toledo Universal Control Box and EasyMax iControl™ software to allow for real-time mass readings throughout the process run. It became apparent through the trial testing that it was beneficial to split the sulfuric

acid used in the process across all three feeds to reduce the level of gas generation from the nitric acid and provide a more comparable flow rate across all three feeds.

To ensure complete conversion of DAPO to LLM-105 prior to the quench, residence time for the reaction was increased by adding a final 100-mL EasyMax CSTR reactor to the reaction process train. A peristaltic pump was used to transfer the reaction mixture to the quench vessel throughout the process. The suction line out of the CSTR was set at a level of 80-mL in the EasyMax reactor. An external temperature control chiller unit was used to circulate water through the heat exchange layers within the AFR during the run as shown in Figure 3. This water acted as the cooling medium for the reaction.

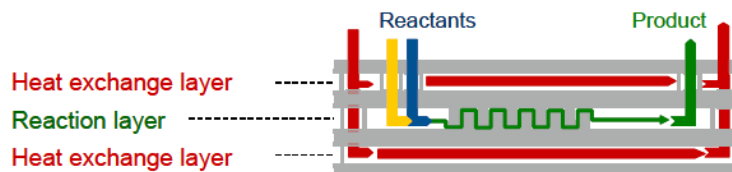


Figure 3. Corning glass reactor plate design

Four temperature probes were inserted into the water coolant circulation loop in the following locations: #1-Reactor A entrance, #2-Reactor A exit, #3-Reactor B entrance, #4-Reactor B exit. The final process design is shown below in Figures 4 and 5.

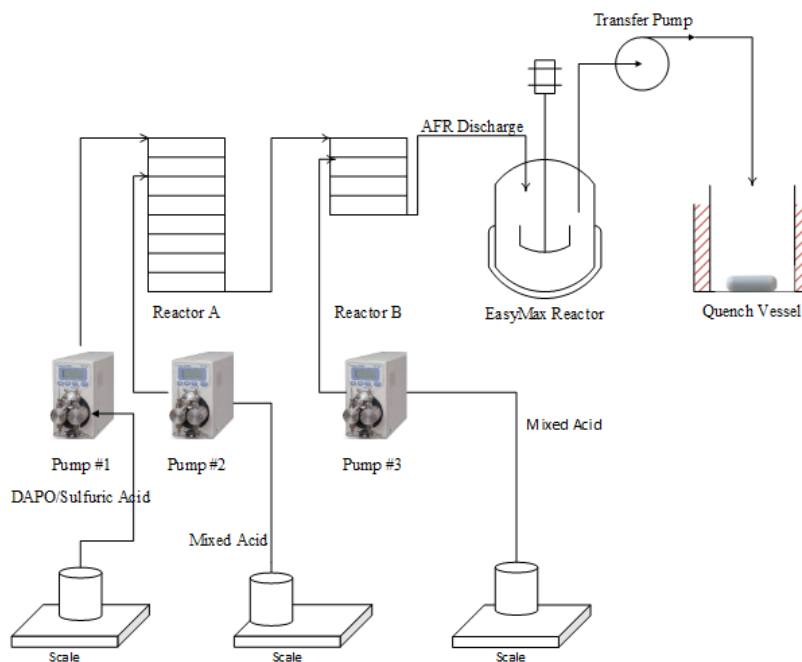


Figure 4. Process design overview

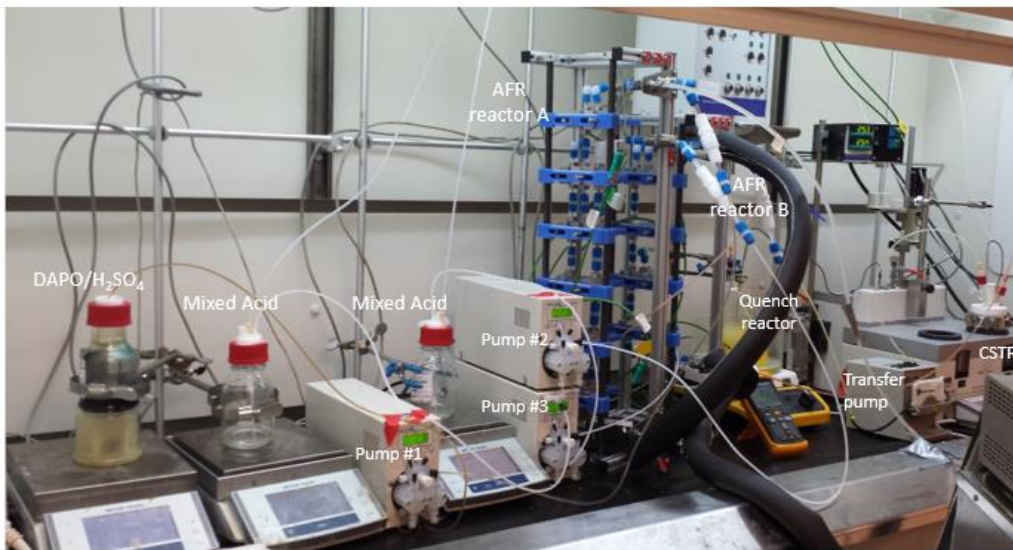


Figure 5. Experimental setup

4.1 Engineering

4.1.1 Kinetic Model Development

A reaction network for the nitration of DAPO to LLM-105 was previously established for the nitration process using concentrated sulfuric acid and fuming nitric acid as reaction media. The set of reactions used in the kinetic model are provided in Table I below.

Table I. Reactions used to fit reaction kinetics

Reaction 1	DAPO + NO ₂ ⁺	→ NDAPO
Reaction 2	NDAPO + NO ₂ ⁺	→ LLM-105
Reaction 3	NDAPO + NO ₂ ⁺ + H ₂ O	→ Decomp1
Reaction 4	DAPO + 2NO ₂ ⁺ + H ₂ O	→ Decomp2

The reactions in Table I were used to build an empirical model. The compounds entitled “Decomp1” and “Decomp2” are included in the model to allow for decomposition reactions of DAPO and NDAPO. It has been found from previous reactions that the material balance is not closed using only the concentrations of DAPO, NDAPO and LLM-105. The compounds entitled “Decomp1” and “Decomp2” are surrogates for the entire decomposition pathways.

The kinetic parameters were fit to the following form of the Arrhenius equation, shown in Equation 1, and the regressed values are listed in Table II.

$$k = k_{ref} * e^{-\frac{Ea}{R} * \left(\frac{1}{T} - \frac{1}{T_{ref}}\right)} \quad (1)$$

Table II. Kinetic parameters for LLM-105 nitration using T_{ref} as 15°C and the reactions listed in Table I.

Reaction	k_{ref}	Units	E_a	Units
1	1.80E-02	L/mol.s	34.01	kJ/mol
2	1.16E-03	L/mol.s	49.93	kJ/mol
3	2.20E-04	L ² /mol ² .s	61.74	kJ/mol
4	1.60E-03	L ³ /mol ³ .s	50.00	kJ/mol

4.1.2 Process Model

The regressed kinetic parameters were used to construct a model using the software DynoChem[®]. The model was specific for nitration reaction in the AFR. The reactor was modeled as a tubular reactor with perfect mixing. Simulation of the reaction in a tube produced the result shown in Figure 6 below. Flow rates for the feeds in the AFR were chosen to be within the limitations of the pumps and also with a goal of producing NDAPO within the AFR. It should be noted that the minimum flow rate Corning recommends for the low flow reactor is 1 ml/min and maximum feed rate is 10 ml/min total flow. We identified a minimum flow rate for each mixed acid feed at 0.25 ml/min. Previous experiments have shown that the highest heat output for the reaction is during the NDAPO formation step and the reaction heat begins to subside after the NDAPO conversion is maximized. Using the AFR to control exothermic reactions is one of the advantages of the system. The residence time to enter the CSTR from the AFR was 9.37 min based on a flow rate of 0.48 ml/min for the DAPO/sulfuric acid feed and 0.25 ml/min for each of the two mixed acid feeds. We applied our model to predict concentrations of NDAPO and LLM-105 in the discharge from the AFR (Table III).

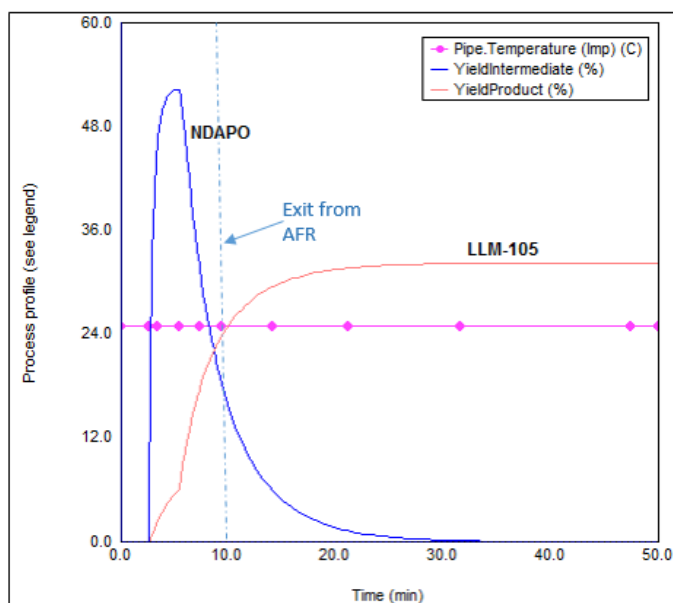


Figure 6. Dynochem process model simulation of LLM-105 reaction in a PFR

Table III. Expected conversion data upon exit of the reaction stream from the AFR

Time min	Pipe	Variables	Variables
	Temperature (Im C	YieldIntermediat %	YieldProduct %
9.259		18.733	23.613
9.309		18.496	23.722
9.359		18.262	23.83
9.373	25.0	18.198	23.859
9.409		18.031	23.936
9.459		17.804	24.04
9.51		17.58	24.143
9.56		17.36	24.244

4.1.3 Model Validation

The AFR was filled with sulfuric acid prior to starting the reaction. Once the three reactant feeds were started, they displaced the sulfuric acid with the nitration reaction mixture. The residence time of the AFR was 8.20 min during the run, which provided 36.6 turnovers of the AFR. The high level of turnover leaves little doubt that the material exiting the AFR should have been in a steady state condition early in the run; however, as explained below, there are reasons why the steady state condition within the AFR may have been less than ideal. The CSTR was started up as an empty reactor. To eliminate the possibility of diluting the CSTR initially with the sulfuric acid in the AFR, the discharge line out of the AFR was not originally positioned to feed into the CSTR but into an acid waste container. When it became apparent that the nitration reaction was taking place within the AFR, the discharge tubing out of the AFR was repositioned to feed the CSTR. The residence time of the CSTR was 81.55 min, which provided 3.68 turnovers of the contents. This residence time would allow enough time to achieve steady state within the CSTR. The actual mass flow rate of the DAPO solution and the mixed acids was logged and compared to desired flow rates over the course of the experiment, ensuring that the reaction was running at the desired stoichiometry. The flow rates in Figure 7 showing the data recorded in the iControl™ EasyMax software are averaged to remove some of the noise from the data. Axis 1 displays the average flow rate for both mixed acid feeds along with a blue line denoting the desired flow rate for these two feeds. Axis 2 displays the average DAPO solution feed rate along with a red line denoting the desired flow rate for the DAPO solution feed.

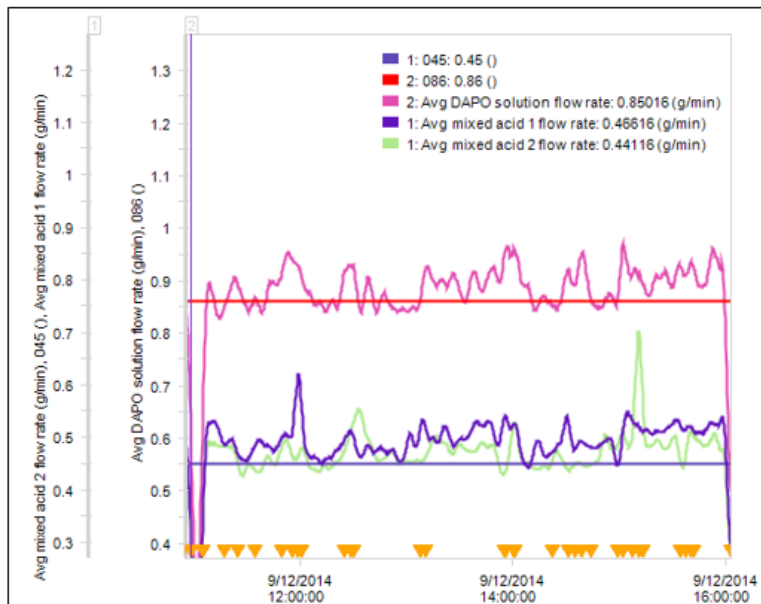


Figure 7. iControl data showing mass flow rates versus desired flow rates during the run

Temperature data within the AFR was logged manually during the experiment and is shown in Table IV below. As expected, no temperature differential existed across the AFR reactor platform during the process. The exceptional heat transfer across the AFR allows for the nitration reaction to be completed with little concern for temperature gradients in the AFR.

Table IV. Temperature during the process run at four points within the AFR

Time	Temperature ($^{\circ}\text{C}$)			
	Reactor A entrance	Reactor A exit	Reactor B entrance	Reactor B exit
0	24.7	24.6	24.9	24.8
12	24.9	25	25	24.8
26	25	25	25	24.8
48	25.1	25	25	24.9
86	25	25.1	25	24.9
123	25	25.1	25	24.8
161	25.1	25.2	25.1	24.9
205	25.2	25.4	25.2	24.9
288	25.3	25.3	25.3	25

Samples were pulled throughout the reaction to determine concentration of NDAPO and LLM-105 upon exit from the AFR and also within the CSTR during the run. A comparison of the process model with the experimental data was promising if not in complete agreement. Referring to Figure 8 below, the process model simulation accurately predicted that upon exiting the AFR, the DAPO would have been consumed and NDAPO would have been converting to LLM-105. The in-situ yield of the LLM-105 both exiting the AFR and in the CSTR was higher than predicted by the kinetic model. The yields, being in the 40–45% range, offer an encouraging initial result in running the reaction in a plug flow reactor setup. The semi-batch reaction typically results in yields at or around 50% when using sulfuric acid. Reconfiguring the

number of mixed acid feeds and the exact location of the feeds within the plug flow reactor would allow for future optimization of the yield out of the AFR.

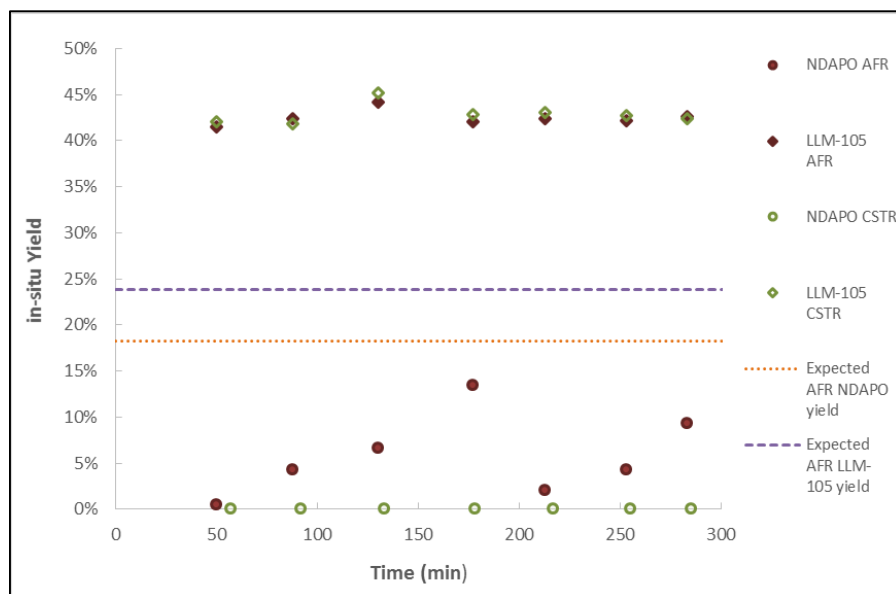


Figure 8. In-situ yield of NDAPO and LLM-105 exiting the AFR and in the CSTR

The conversion data collected from the exit of the AFR showed steady conversion to LLM-105 across all samples in contrast to the NDAPO conversion data, which never appeared to reach a consistently steady level. In both cases, the data suggests that the reaction kinetics ran faster than predicted by the model. It should be noted that during this experiment, at the initial mixing point of the DAPO solution feed and the first mixed acid feed, only 75% of the sulfuric acid is present as part of the reaction stream. The final 25% of the sulfuric acid is introduced in the final mixed acid feed. The accelerated reaction kinetics could be attributed to the more concentrated reaction conditions at the initial mixing point. The instantaneous introduction of 1.5 molar equivalents of the nitric acid to the DAPO stream is another difference between this experiment and the semi-batch conditions used to generate the kinetic model. The kinetic model used as the basis for this process was developed under a defined design space, and the modifications made for this experiment operate outside of this space. Some nitration reactions are known to possess changing apparent reaction rates constants based on acidity levels within the reaction, so it is not unexpected for the model to not agree entirely with the process result achieved under modified conditions.

The lack of a constant level of NDAPO exiting the AFR can be attributed to several non-ideal conditions within the reactor. The slight but consistent deviations in pump flow rate throughout the run create a scenario in which at each point in time during the run, slight differences in the molar ratio of the reaction components can exist within the reaction stream. Depending on the flow rate of the mixed acids in comparison to the DAPO solution, the reaction can either be lean in nitric acid or have a slight excess beyond the intended three molar equivalents of nitric acid. This molar ratio variation alters the level of conversion expected at the end of the reaction at any one point in time. Reaction off-gassing was also observed during the run, which can have alter flow rates within a plug flow reactor and challenge the establishment of a consistent conversion rate from the AFR. These challenges in running a plug flow reactor at low flow rates highlight an advantage to having a small CSTR at the end of the reactor process train. In the case of this experiment, the CSTR served to dampen out disturbances in flow rates within the

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AFR, enabling consistent conversion to LLM-105 in the CSTR with no remaining NDAPO. The fact that complete NDAPO conversion did not result in a concomitant increase in LLM-105 yield can be explained by competing decomposition pathways; however, complete NDAPO conversion is required to isolate LLM-105 in high purity and these are promising results.

4.2 Material Characterization

4.2.1 Analytcs

In this study, we used three main analytical methods that utilized HPLC. The purity was determined by comparing the isolated LLM-105 to analytical standards of LLM-105 and NDAPO. The quantity of residual inorganics from the acids (e.g. sulfate, nitrate) was determined by Ion Chromatography (IC). The amount of oxamidem a known impurity, was also determined by comparing the isolated LLM-105 to analytical standards of oxamide. Tables V, VI, and VII show the standard conditions for each analytical method.

Table V. HPLC chromatographic conditions for the analysis of LLM-105

CHROMATOGRAPHIC CONDITIONS		
Column: Thermo Scientific Hypercarb 100 mm x 4.6 mm, 5 um, P/N 35005-104630		
Column Temperature: 40° C		
Injection Parameters: Injection Volume: 10 µL		
Flow Rate: 1.0ml/min		
Detection: UV @ 304nm; BW=10; Ref=off		
Run Time: 12 minutes		
Mobile Phase : 85/15 Acetic Acid Glacial/Methanol		
Sample Diluent: Dimethyl Sulfoxide		
Isocratic:	Time (minutes)	% A
	0	100
	12	100

Table VI. Ion chromatographic conditions for the analysis of residual acid salts in LLM-105

IC CHROMATOGRAPHIC CONDITIONS	
Column:	Waters IC-PAK Anion HC, 4.6 mm x 150 mm, PN WAT026770
Column Temperature:	30° C
Injection Parameters:	Injection Volume: 50 µL
Flow Rate:	2.0 ml/min
Detection:	Conductivity detection
Run Time:	35 minutes
Mobile Phase:	12% /2% /86% Acetonitrile/Butanol/Gluconate Buffer

Table VII. HPLC chromatographic conditions for the analysis of residual oxamide in LLM-105

Oxamide CHROMATOGRAPHIC CONDITIONS	
Column:	Thermo Scientific Hypercarb, 4.6 mm x 100 mm, 5um, PN 35005-104630
Column Temperature:	40° C
Injection Parameters:	Injection Volume: 5 µL
Flow Rate:	2.0 ml/min
Detection:	205 nm
Run Time:	7 minutes
Mobile Phase:	100% Water Column flush: 100% 0.1% TFA in acetonitrile at 2.5 mL/min

4.2.2 Characterization

During the process run, quenched LLM-105 was collected for a one-hour time period to obtain a sample for final analysis and to assess the isolated process yield. The dried sample contained 3.23 grams of LLM-105, giving a yield over the hour of 36.2%. Accounting for losses during the

material workup and isolation, this value is consistent with the in-situ yields recorded in the CSTR of 40–45%. A portion of this material was slurried in 65 °C water for three hours for comparison to the material isolated directly from the process. Assuming a 5% loss in the workup, this process setup provides LLM-105 at a rate of 3.39 g/hr with a combined flow rate of all three feeds of 0.981 ml/min.

A full analysis of the LLM-105 prior to and after the rewash was completed. The material after the rewash showed increased potency and the trace amount of sulfate in the prewashed LLM-105 was no longer present in the washed LLM-105. Table VIII shows this analysis.

Table VIII. Final analysis of LLM-105 before the hot water rewash and after the rewash

	% Potency	% Purity	% Oxalate	% NO3-	% SO4-	Oxamide
Prewashed LLM-105	99.4	100	< 0.03%	< 0.03%	< 0.03%*	Not Detected**
Washed LLM-105	99.6	100	< 0.03%	< 0.03%	< 0.03%	Not Detected**

* The IC results for the pre-wash material show a trace level of sulfate was detected (See Appendix A for chromatographs), the level is determined to be less than the limit of quantitation (LOQ) for the method and is therefore reported as <0.03%, the LOQ for the method. Sulfate was not detected in the washed material and is reported as <0.03% per the method LOQ reporting criteria.

**~0.05% Detection limit estimated

5.0 Conclusions

In this work, Nalas designed and tested a process for performing a continuous energetic nitration reaction in an AFR, producing LLM-105 of high potency. The reaction achieved extremely promising in-situ yields for a first run in the 40–45% range. The ability to scale this technology offers an avenue to achieving a manufacturing level of production. With additional effort, future improvements could be made to the process. The acquisition of larger scale flow reactors would allow the reaction to be completed at higher flow rates in the future, eliminating some of the challenges experienced in controlling the pump flow rates at the low end of the pumps' recommended flow rate range. Operating at higher flow rates should also decrease variability in the stoichiometry of the reaction across the AFR. Both the size and presence of a CSTR in the reactor process train could be modified. With the right design, it should be possible to eliminate it, thereby reducing the complexity and equipment requirements for the process. The quench reactor design should be a focus in future process design improvements as optimization of the quench would ensure high quality product directly from the reaction. Eliminating the need to reslurry isolated LLM-105 in water would be an added benefit, reducing the cost at larger scales. Finally, expansion of the kinetic model to include operating conditions expected in the continuous production run, specifically various levels of sulfuric acid to account for the nitric acid being dosed as a nitric-sulfuric mixed acid, would improve the performance of the model and allow identification of conditions that are problematic for smooth conversion of DAPO to LLM-105.